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**Robust Summaries
for
Propylene Carbonate
CAS Number 108-32-7**

USEPA HPV Challenge Program Submission

April 10, 2002

Submitted by:

Propylene Carbonate / t-Butyl Alcohol HPV Committee

Members:

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Propylene Carbonate

High Production Volume

Robust Summaries of Existing Studies

PHYSICAL/CHEMICAL ELEMENTS

Data Point	Method	Value
1) MELTING POINT	Not Stated	-48.8 °C
Reference: Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79 th ed. Boca Raton, FL: CRC Press Inc. 1998-1999, p. 3-145.		
2) BOILING POINT	Not Stated	242 °C
Reference: Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79 th ed. Boca Raton, FL: CRC Press Inc. 1998-1999, p. 3-145.		
3) VAPOUR PRESSURE	Not Stated	0.045 mm Hg
Reference: Daubert, T.E., Danner, R.P. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, DC, Taylor and Francis, 1989.		
4) PARTITION COEFFICIENT	Not stated	Log Pow: -0.41 Temp: Not stated
Reference: Hansch, C., Leo, A., Hoekman, D., 1995. Exploring QSAR – Hydrophobic, Electronic, and Steric Constants. Washington, DC, American Chemical Society, p. 9.		
5) WATER SOLUBILITY	Not Stated	175,000 mg/l @ 25 °C
Reference: Riddick, J.A., Bunger, W.B., Sakano, T.K., 1985. Techniques of Chemistry 4 th ed., Volume II. Organic Solvents. New York, NY, John Wiley and Sons, p. 434.		
6) PHOTODEGRADATION	Calculated	Half-life t _{1/2} (preferred): 4 days
Sensitizer (type) – hydroxyl radicals Rate Constant : 4.7x10 ⁻¹² cu cm/molecule-sec @ 25 °C		
Reference: Meylan, W.M., Howard, P.H., 1993. Chemosphere 26: 2293-2299.		

9) BIODEGRADATION

TEST SUBSTANCE

Identity: Propylene carbonate

METHOD

Method/guideline followed: Manostatic respirometer screening study

Test Type (test type/aerobic/anaerobic): Aerobic

GLP (Y/N): No data

Year (study performed): Not stated

Contact time (units): 10 days

Innoculum: Seed from wastewater treatment plant

Remarks field for Test Conditions:

- Concentration of test chemical, vehicle used, pre-acclimation conditions: Not stated
- Temperature of incubation °C: Not stated
- Dosing procedure: Not stated
- Sampling frequency: Not stated
- Appropriate controls and blank system used? Not stated
- Analytical method used to measure biodegradation: Not stated
- Method of calculating measured concentrations (i.e., arithmetic mean, geometric mean, etc.): Not stated

RESULTS

Degradation % after time: 80 % during a 10-day period

- For each time period %: Not stated

Breakdown products (yes/no) If yes describe breakdown products and whether they were transient or stable in the Remarks field for Results. Not stated

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: Submitter concludes that propylene carbonate is readily biodegradable.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 2, key study
Remarks field for Data Reliability: Not standard test; limited details available

REFERENCES (Free Text)

Kayser, G et al., 1993. Git Fachz Lab 37: 416-419

OTHER

Last changed (administrative field for updating): 3/11/02 by ToxWorks

ECOTOXICITY ELEMENTS

10) ACUTE TOXICITY TO FISH

TEST SUBSTANCE

Identity : n-Butylene carbonate

Remarks field for Test Substance: analog of Propylene carbonate

METHOD

Method/guideline followed (experimental/calculated): OECD 203

Type (test type): Semistatic, daily renewal

GLP (Y/N): Yes

Year (study performed): 1988

Species/Strain/Supplier: Rainbow trout (*Salmo gairdneri*), Parkwood Trout Farm, Kent, UK

Analytical monitoring: Yes

Exposure period (unit): 96 hours

Statistical methods: Thompson and Weil, 1952. Biometrics 8: 51-54.

Remarks field for Test Conditions:

- Test fish (Age/length/weight, loading, pretreatment) - Test conditions, e.g.: age- not given, length – 6.4 ± 0.3 cm, weight- 3.96 ± 0.8 g, acclimated to lab 17 days, acclimated to test conditions 7 days
- Details of test (static, semi-static, flow-through): Daily renewal
- Dilution water source: Laboratory tap water, dechlorinated
- Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity): hardness – 350 mg/l as CaCO_3 ,
- Stock and test solution and how they are prepared: 100, 180, 320, 560, and 1000 mg/l – direct dispersion into water
- Stability of the test chemical solutions: Verified by chemical analysis
- Exposure vessel type (e.g., size, headspace, sealed, aeration, lighting, # per treatment): Glass aquaria holding 40 l of test media
- Number of replicates, fish per replicate: 1 replicate of 10 fish per concentration
- Water chemistry in test (D.O., pH) in the control and one concentration where effects were observed: DO = 9.6 – 10.1 in control; 9.5 – 10.1 in treatment groups; pH 7.8–7.9
- Test temperature range - Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): 14.0 °C at all measurement times

RESULTS

Nominal concentrations (as mg/L): 0, 100, 180, 320, 560, 1000

Measured concentrations (as mg/L): <2.7 (loq), 103, 150, 318, 534, 875 at 0 hrs
<2.7 (loq), 99, 167, 338, 524, 907 at 24 hrs
<2.7 (loq), 97, 162, 313, 565 at 96 hrs

Element value (e.g. LC50, LCo, LL50, or LL0 at 48, 72 and 96 hours, etc., based on measured or nominal concentrations): LC50 at 48 = 510 (410-620), 72 = 480 (400-580), and 96 = 480 (400-580) mg/l based on nominal concentration.

Remarks field for Results:

- Biological observations: Hyperactive, swimming at surface, increased pigmentation, loss of equilibrium

- Table showing cumulative mortality:

(mg/l)	hours: 6	24	48	72	96
control	0	0	0	0	0
100	0	0	0	0	0
180	0	0	0	0	0
320	0	0	0	0	0
560	1	2	7	8	8
1000	4	10	10	10	10

- Lowest test substance concentration causing 100% mortality: 1000 mg/l
- Mortality of controls: 0
- Reference substances (if used) - results: None used

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: Submitter concludes low acute toxicity to fish from butylene carbonate and therefore also expected for propylene carbonate.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, key study

REFERENCES (Free Text)

Douglas, M.T., Sewell, I.A., Macdonald, I.A., 1989. The Acute toxicity of n-Butylene carbonate to rainbow trout (*Salmo gairdneri*). Huntingdon Life Sciences Report TXO 11 (c) /89488, pp. 1-14.

OTHER

Last changed (administrative field for updating): 3/11/02 by ToxWorks

12) ACUTE TOXICITY TO AQUATIC INVERTEBRATES (E.G., DAPHNIA)

TEST SUBSTANCE

Identity: n-Butyl carbonate

Remarks field for Test Substance: Analog of propylene carbonate

METHOD

Method/guideline followed (experimental/calculated): OECD 202 Part 1

Test type: Acute toxicity (immobilization)

GLP (Y/N): Yes

Year (study performed): 1988

Analytical procedures: Yes

Species/Strain: *Daphnia magna* (Straus)

Test details (static, semi-static, dosing rate, flow-through rate, etc.): Static

Statistical methods: No

Remarks field for Test Conditions:

- Test organisms:

- source, supplier, any pretreatment, breeding method: Laboratory culture derived from strain supplied by IRCHA in France. Reproduction by parthenogenesis

- Age at study initiation: less than 24 hours

- Control group: Yes
- Test conditions:
- Stock solutions preparation (vehicle, solvent, concentrations) and stability: Direct dispersion at 1000 mg/l
- Test temperature range: 22.0 °C
- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): Glass jars containing 200 ml of test solution
- Dilution water source: Dechlorinated tap water
- Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio): 350 mg/l as CaCO₃, pH 8.
- Lighting (quality, intensity and periodicity): 16 hrs light/8 dark
- Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed: DO = 9.4 – 9.8 mg/l, pH – 8.
- Element (unit) basis (i.e. immobilization): Immobilization
- Test design (number of replicates, individuals per replicate, concentrations): 4 replicates of 10 organisms in control and treated groups
- Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Not stated
- Exposure period : 48 hours
- Analytical monitoring : Yes

RESULTS

Nominal concentrations in mg/L: 1000 mg/l

Measured concentrations in mg/L: 910 and 964 at 0 hrs; 844 and 903 at 48 hrs

Unit [results expressed in what unit]: mg/l

EC50, EL50, LC0, LL0, at 24, 48 hours: >1000 mg/l

Statistical results, as appropriate

Remarks field for Results:

- Biological observations:
- Number immobilized as compared to the number exposed: No effects
- Cumulative immobilization: Zero

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or

submitter: Submitter concludes low acute toxicity to daphnia from butylene carbonate and therefore also expected for propylene carbonate.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, key study

REFERENCES (Free Text)

Douglas, M.T., Sewell, I.A., Macdonald, I.A., 1989. The Acute toxicity of n-Butylene carbonate to Daphnia magna. Huntingdon Life Sciences Report TXO 11 (b) /89505, pp. 1 - 13.

OTHER

Last changed (administrative field for updating): 3/11/02 by ToxWorks

HEALTH ELEMENTS

13a) ACUTE TOXICITY

TEST SUBSTANCE

Identity: Propylene carbonate

METHOD

Method/guideline followed (experimental/calculated): equivalent to EPA 870.1100

Type (test type): Acute lethality

GLP (Y/N): Yes

Year (study performed): 1985

Species/Strain: Sprague-Dawley rats

Sex: Both

No. of animals per sex per dose: 5

Vehicle: None

Route of administration (if inhalation - aerosol, vapor, gas, particulate): Oral

Remarks field for Test Conditions:

- Age (Not reported) – Weight 180-219 g after fasting.
- Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail) – 5000 mg/kg
- Doses per time period – One dose
- Volume administered or concentration: As received
- Post dose observation period: 14 days

RESULTS

Value [LD50 or LC50] with confidence limits if calculated: >5000 mg/kg

Number of deaths at each dose level: None

Remarks field for Results:

- Description, severity, time of onset and duration of clinical signs at each dose level:
No clinical signs
- Necropsy findings, included doses affected, severity and number of animals affected:
No abnormalities in any animal

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter. Submitter concludes that propylene carbonate is practically non-toxic from acute oral exposure.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1; key study

REFERENCES (Free Text)

Mallory, V.T., Naismith, R.W., Matthews, R.J., 1985. Acute Oral Toxicity Study in Rats (14 day), Pharmakon Research International Final Report PH 402-TX-004-85, pp. 1-13.

OTHER

Last changed (administrative field for updating): 11/21/01 by ToxWorks

13b) ACUTE TOXICITY

TEST SUBSTANCE

Identity: Propylene carbonate

METHOD

Method/guideline followed (experimental/calculated): Equivalent to EPA 870.1200

Type (test type): Acute lethality

GLP (Y/N): Yes

Year (study performed): 1986

Species/Strain: New Zealand White Rabbits

Sex: Both

No. of animals per sex per dose: 5

Vehicle: None

Route of administration (if inhalation - aerosol, vapor, gas, particulate): Dermal

Remarks field for Test Conditions:

- Age (Not reported) – Weight 2-3 kg.
- Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail) – 3000 mg/kg applied to abraded skin and occluded for 24 hours.
- Doses per time period – One dose
- Volume administered or concentration: As received
- Post dose observation period: 14 days

RESULTS

Value [LD50 or LC50] with confidence limits if calculated: >3000 mg/kg

Number of deaths at each dose level: None

Remarks field for Results:

- Description, severity, time of onset and duration of clinical signs at each dose level:
No clinical signs
- Necropsy findings, included doses affected, severity and number of animals affected:
No abnormalities in any animal

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter. Submitter concludes that propylene carbonate is practically non-toxic following a single dermal exposure.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1

REFERENCES (Free Text)

Mallory, V.T., Matthews, R.J., 1986. Acute Dermal Toxicity Test in Rabbits (14 day), Pharmakon Research International Final Report PH 422-TX-006-86, pp. 1-15.

OTHER

Last changed (administrative field for updating): 9/10/01 by ToxWorks

GENETIC TOXICITY ELEMENTS

14) GENETIC TOXICITY IN VIVO (CHROMOSOMAL ABERRATIONS)

TEST SUBSTANCE

Identity: Propylene carbonate

METHOD

Method/guideline followed: Equivalent to EPA 870-5395

Type (test type): Micronucleus in mice

GLP (Y/N): Yes

Year (study performed): 1985

Species: Mouse

Strain: CRL CD-1

Sex: Both

Route of administration (if inhalation - aerosol, vapor, gas, particulate): Intraperitoneal injection

Doses/concentration levels: 1666 mg/kg

Exposure period: Single injection; subgroups were exposed for 30, 48 and 72 hours

Statistical methods: One-tailed t-test

Remarks field for Test Conditions:

- Age at study initiation: Seven and one-half weeks
- No. of animals per dose: 15 males and 15 females (5 for each time point): retest including 10 male and 10 female exposed for 72 hours only
- Vehicle: Distilled water
- Duration of test: 72 hours
- Frequency of treatment : Once
- Sampling times and number of samples: 30, 48, and 72 hours
- Control groups and treatment: Untreated control, positive control (TEM), one dose level of test material
- Clinical observations performed (clinical pathology, functional observations, etc.): Toxic signs
- Organs examined at necropsy (macroscopic and microscopic): Not stated
- Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test): 1000 PCEs
- Criteria for selection of M.T.D.: Highest non-lethal dose in preliminary test

RESULTS

Effect on mitotic index or PCE/NCE ratio by dose level by sex:

	MN/1000 PCE	PCE/NCE
H2O	0.20±0.42	1.61±0.55
TEM	54.23±16.78*	0.77±0.18*
PC-30 hr	0.50±0.97	1.76±0.42
PC-48 hr	0.30±0.48	1.43±0.50
PC-72 hr	1.20±1.40*	1.59±.037
Repeat		
H2O	0.50±0.85	1.92±0.48
TEM	48.5±9.03*	0.83±0.20*
PC-72 hr	0.30±0.57	1.77±.064

Genotoxic effects (positive, negative, unconfirmed, dose-response, equivocal):

Negative

NOAEL(NOEL) (C)/LOAEL(LOEL) (C)

Statistical results, as appropriate: * = statistically significant at $p < 0.05$

Remarks field for Results: Because positive result obtained only at 72 hours and not confirmed in repeat test with larger animal population (10/sex instead of 5/sex), the authors judged the results to be negative.

- Mortality at each dose level by sex: None
- Mutant/aberration/mPCE/polyploidy frequency, as appropriate: See table above
- Description, severity, time of onset and duration of clinical signs at each dose level and sex: Writhing after dosing; decreased body tone in some animals
- Body weight changes by dose and sex: No significant changes
- Food/water consumption changes by dose and sex: Not recorded

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: The authors concluded the study was negative.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1; key study

REFERENCES (Free Text)

Sorg, R.M., Naismith, R.W., Matthews, R.J., 1986. Micronucleus Test (MNT) – OECD, Pharmakon Research International, Inc. Final Report PH 309A-TX-004-85, pp. 1-58.

OTHER

Last changed (administrative field for updating): 3/11/02 by ToxWorks

15) GENETIC TOXICITY IN VITRO (GENE MUTATIONS)

TEST SUBSTANCE

Identity: Propylene carbonate

METHOD

Method/guideline followed: Ames method, equivalent to EPA 870-5100 except did not test *E.coli*.

Type (e.g. reverse mutation assay, gene mutation study, cytogenetic assay, mammalian cell gene mutation assay, cytogenetic assay, etc.): Reverse mutation - Ames

System of testing [bacterial, non bacterial]: Bacterial

GLP (Y/N): Yes

Year (study performed): 1985

Species/Strain or cell type and or cell line, bacterial or non-bacterial: Salmonella, TA98, TA100, TA 1535, TA1537, TA1538

Metabolic activation: S-9 from liver of Sprague-Dawley rats treated with Aroclor 1254

- Species and cell type

- Quantity

- Induced or not induced

Concentrations tested: 50, 167, 500, 1667, and 5000 ug/plate as preincubation assay

Statistical Methods: Moore and Felton, 1983. Mutat. Res. 119: 95-102.

Remarks field for Test Conditions:

- Test Design

· Number of replicates: Three

- Frequency of Dosing: Pre-incubation assay
- Criteria for evaluating results (e.g. cell evaluated per dose group): triple untreated control rate or statistically significant trend

RESULTS

Result:

Cytotoxic concentration:

- With metabolic activation: >5000 µg/plate
- Without metabolic activation: >5000 µg/plate

Genotoxic effects (e.g. positive, negative, unconfirmed, dose-response, equivocal):

- With metabolic activation: Negative
- Without metabolic activation: Negative

Statistical results, as appropriate:

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or

submitter: The authors concluded that the test material was negative in the Ames assay.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, key study

REFERENCES (Free Text)

Godek, E.G., Naismith, R.W., Matthews, R. J., 1985. Ames Salmonella/Microsome Liquid Pre-Incubation Assay. Pharmakon Research International Inc Final Report PH 301-TX-006-85, pp. 1-22.

OTHER

Last changed (administrative field for updating): 9/14/01 by ToxWorks

16a) REPEATED DOSE TOXICITY

TEST SUBSTANCE

Identity: Propylene carbonate

METHOD

Method/guideline followed: Equivalent to OECD 408

Test type: 90 day Oral Study

GLP (Y/N): Yes

Year (study performed): 1988

Species: Rat

Strain: Charles River Sprague-Dawley derived

Route of administration, oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapor, gas, particulate), other: Gavage

Duration of test : 90 Days

Doses/concentration levels: 0, 1000, 3000, 5000 mg/kg/day

Sex: Both

Exposure period: 90 days

Frequency of treatment: Five days/week for 13 weeks

Control group and treatment : Distilled water by gavage

Post exposure observation period: Additional groups of control and high-dose observed for 28 days post dosing.

Statistical methods: One-way analysis of variance, followed by Dunnett's or Tukey's tests.

Remarks field for Test Conditions:

- Test Subjects:

- Age at study initiation: 40 days
- No. of animals per sex per dose- Study Design: 10, additional 5/sex/dose terminated after 30 days; additional 10/sex for control and high dose held 28 days post dosing.
- Vehicle: None, dosed as received.
- Satellite groups and reasons they were added: Control and high-dose for recovery.
- Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Daily observations, hematology (RBC, Hemat., PCV, WBC, diff., plt) and clinical chemistry (glu, crea, tbil, bun, ALT, AST, GGT, Tpro, alb, glob, Na, K, Cl, Ca, P) at 30 and 90 days. Ophthalmoscopy pretest at 30 and 90 days.
- Organs examined at necropsy (macroscopic and microscopic): brain, pituitary, thyroid, parathyroid, thymus, lungs, trachea, heart, sternum with bone marrow, salivary glands, liver, spleen, kidneys, adrenals, pancreas, gonads, uterus, accessory sex organs, aorta, skin, esophagus, nasal turbinates, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, urinary bladder, lymph node, mammary gland, skeletal muscle, peripheral nerve, three levels of spinal cord, lachrymal glands.

RESULTS

NOAEL (NOEL): 5000 mg/kg/day

LOAEL (LOEL)

Actual dose received by dose level by sex, if known,

Toxic response/effects by dose level: No adverse effects seen

Statistical results, as appropriate:

Remarks field for Results:

- Body weight: No treatment effect
- Food/water consumption: No treatment effect
- Description, severity, time of onset and duration of clinical signs: No treatment effect
- Ophthalmologic findings incidence and severity: No treatment effect
- Hematological findings incidence and severity: No treatment effect
- Clinical biochemistry findings incidence and severity: Few clinical chemistry significant differences, not consistent between sexes or 30 vs. 90 days

- Mortality and time to death: No treatment effect
- Gross pathology incidence and severity: No treatment effect
- Organ weight changes: Few organ weight differences, not consistent between sexes or 30 vs 90 days
- Histopathology incidence and severity: No treatment effect

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: Authors concluded there were no treatment-related effects.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, key study

REFERENCES (Free Text)

Margitich, D.J., 1989. Subchronic Oral toxicity in Rats. Pharmakon Research International, Inc. Final Report Ph 470-TX-001-88, pp. 1 – 158, plus two appendices.

OTHER

Last changed (administrative field for updating): 3/11/02 by ToxWorks

16b) REPEATED DOSE TOXICITY

TEST SUBSTANCE

Identity: Propylene carbonate

METHOD

Method/guideline followed: Equivalent to OECD 408

Test type: 14 Week Aerosol Inhalation Study

GLP (Y/N): Yes

Year (study performed): 1991

Species: Rat

Strain: Harlan F344

Route of administration, oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapor, gas, particulate), other: Aerosol inhalation

Duration of test : 93 Days

Doses/concentration levels: 0, 100, 500, 1000 mg/m³; diameter (MMAD) = 4.9 microns +/- 2.5 gsd

Sex: Both

Exposure period: 93 days

Frequency of treatment: Six hours/day five days/week for 13 weeks

Control group and treatment : Clean air

Post exposure observation period: No

Statistical methods: One-way analysis of variance, followed by Dunnett's or Tukey's tests.

Remarks field for Test Conditions:

- Test Subjects:

• Age at study initiation: 47 days

• No. of animals per sex per dose - Study Design: 10, additional 5/sex/dose for neurotoxicity evaluation; additional 2/sex for control and high dose for neurotoxicity evaluation after a single exposure.

• Vehicle: None

• Satellite groups and reasons they were added: Control and high dose for neurotoxicity evaluation after a single exposure.

• Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Daily observations, hematology (RBC, Hemat., PCV, WBC, diff., plt) and clinical chemistry (glu, crea, tbil, cbil, ubil, bun, ALT, AST, GGT, SDH, ALK, Tpro, alb, glob, Na, K, Cl, Ca, P) at 90 days. Ophthalmoscopy pretest and 90 days, food and water consumption first 4 weeks, body weights weekly. FOB and motor activity after six and thirteen weeks. FOB one and 23 hours after single 6-hour exposure. For FOB, animals were placed in clean clear cage for 2 minutes while observed for horizontal and vertical movement, convulsions, tremors, stereotypy, piloerection, respiration, urination, gait, and acoustic startle response. The animal was removed and observed for pupil size and response to light, vocalization, salivation, mouthbreathing, lacrimation, diarrhea, visual placing and muscle tone. Catatonia, forelimb and hindlimb grip strength, surface and air righting reflexes performance on a rotating treadmill, positive geotropism, toe and tail withdrawal reflexes, hind leg splay, and rectal temperature were recorded using simple equipment. Motor activity was determined using San Diego Instruments test equipment.

• Organs examined at necropsy (macroscopic and microscopic): brain, pituitary, thyroid, parathyroid, thymus, lungs, trachea, esophagus, nasopharyngeal tissues, larynx, heart, sternum with bone marrow, salivary glands, liver, spleen, kidneys, adrenals, pancreas, gonads, uterus, accessory sex organs, aorta, skin, nasal turbinates, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, urinary bladder, lymph node, mammary gland, skeletal muscle, peripheral nerve, three levels of spinal cord, lachrymal glands, Zymbal's glands.

RESULTS

NOAEL (NOEL): 100 mg/m³

LOAEL (LOEL)

Actual dose received by dose level by sex, if known,

Toxic response/effects by dose level: Inflammation of ocular tissues in 2 males at 500 and 4 males at 1000 mg/m³.

Statistical results, as appropriate:

Remarks field for Results:

- Body weight: No treatment effect

- Food/water consumption: No treatment effect

- Description, severity, time of onset and duration of clinical signs: Periocular swelling at 500 and 1000 mg/m³
- Ophthalmologic findings incidence and severity: No treatment effect
- Hematological findings incidence and severity: No treatment effect
- Clinical biochemistry findings incidence and severity: No treatment effect
- Mortality and time to death: No treatment effect
- Gross pathology incidence and severity: No treatment effect
- Organ weight changes: Few organ weight differences, not consistent between sexes or supported by histopathologic findings.
- Histopathology incidence and severity: No treatment effect

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: Authors concluded there was mild eye irritation at 500 and 1000 mg/m³.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, key study

REFERENCES (Free Text)

Burleigh-Flayer, H.D., Nachreiner, D.J., Kintigh, W.J., 1991. Propylene carbonate: Fourteen-Week aerosol inhalation study on rats with neurotoxicity evaluation. Bushy Run Research Center Final Report 52-637, pp. 1 – 56, plus 12 appendices.

OTHER

Last changed (administrative field for updating): 3/07/02 by ToxWorks

16c) REPEATED DOSE TOXICITY

TEST SUBSTANCE

Identity: Propylene carbonate

METHOD

Method/guideline followed:

Test type: Dermal Carcinogenicity Study

GLP (Y/N): Yes

Year (study performed): 1987-1991

Species: Mouse

Strain: Jackson C3H/HeJ

Route of administration, oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapor, gas, particulate), other: dermal

Duration of test : 104 weeks

Doses/concentration levels: 0, 50 µl/mouse twice/week (~1500-2000 mg/kg/dose)

Sex: Male

Exposure period: 104 weeks

Frequency of treatment: Twice/week for 104 weeks

Control group and treatment : No treatment

Post exposure observation period: No

Statistical methods: One-way analysis of variance.

Remarks field for Test Conditions:

- Test Subjects:

· Age at study initiation: 8 weeks

· No. of animals per sex per dose: 50 males only

· Vehicle: None

· Satellite groups and reasons they were added: None

· Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Daily observations, body weights weekly.

· Organs examined at necropsy (macroscopic and microscopic): Necropsy: Carcass and muscular/skeletal systems, external surfaces and orifices, cranial cavity and brain, neck and associated organs, thoracic, abdominal and pelvic cavities and organs. Microscopic Examination: Skin, nodules, masses and lesions.

RESULTS

NOAEL (NOEL): 1500-2000 mg/kg (twice/week)

LOAEL (LOEL)

Actual dose received by dose level by sex, if known,

Toxic response/effects by dose level: None reported

Statistical results, as appropriate:

Remarks field for Results:

- Body weight: No treatment effect

- Food/water consumption: Not measured

- Description, severity, time of onset and duration of clinical signs: No treatment effect

- Ophthalmologic findings incidence and severity: Not measured

- Hematological findings incidence and severity: Not measured

- Clinical biochemistry findings incidence and severity: Not measured

- Mortality and time to death: No treatment effect

- Gross pathology incidence and severity: No treatment effect

- Organ weight changes: Not measured

- Histopathology incidence and severity: No treatment effect

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: Authors concluded there was no increase in tumors.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, Key study

REFERENCES (Free Text)

Garman, R.H., Van Miller, J.P., Negley, J.E., 1991. Chronic Dermal Carcinogenicity Studies in C3H/HeJ Male Mice. Bushy Run Research Center Final Report 52-527, pp. 1–143, plus 8 appendices.

OTHER

Last changed (administrative field for updating): 9/11/01 by ToxWorks

17) TOXICITY TO REPRODUCTION

TEST SUBSTANCE

Identity: Propylene Carbonate

METHOD

Method/guideline followed: Assessment of reproductive organs in a 90 day study

Type (one generation, two generation, etc.): 90 Day Oral, Evaluation of Sex organs

GLP (Y/N): Yes

Year (study performed): 1988

Species: Rat

Strain: Charles River Sprague-Dawley derived

Route of administration - oral (gavage, drinking water, feed), dermal, inhalation
(aerosol, vapor, gas, particulate), other: Gavage

Doses/concentration levels: 0, 1000, 3000, 5000 mg/kg/day

Sex: Both

Control group and treatment: Yes

Frequency of treatment: Five days/week

Duration of test: 13 weeks

Premating exposure period for males (P and F1) as appropriate

Premating exposure period for females (P and F1) as appropriate

Statistical methods: One-way analysis of variance, followed by Dunnett's or Tukey's tests.

Remarks field for Test Conditions:

- Test animals:

• Number, age, sex per dose for P, F1 and F2, if appropriate: 10/sex/group at 40 days old

- Test design:

• Vehicle: None

• Dosing schedules and pre and post dosing observations periods for P, F1 and F2, if appropriate: Five days/week

- Parameters assessed during study P and F1 as appropriate:

- Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Daily observations, hematology. Clinical chemistry at 30 and 90 days
- Estrous cycle length and pattern (number of days spent in each phase): Not assessed
- Sperm examination (epididymal or vas sperm, concentration, motility, morphology): Not assessed
- Parameters assessed during study F1 and F2, as appropriate:
- Clinical observations performed and frequency (weight gain, growth rate, etc.): Weekly BW
- Organs examined at necropsy (macroscopic and microscopic): Ovaries, uterus, testes, accessory sex organs

RESULTS

NOAEL (NOEL) and LOAEL (LOEL) for P, F1 and F2, as appropriate: 5000 mg/kg/day

Actual dose received by dose level by sex if known

Statistical results, as appropriate

Remarks field for Results: Assessment of reproductive organs from 90 day study

- Body weight: No treatment effect
- Food/water consumption: No treatment effect
- Description, severity, time of onset and duration of clinical signs: No treatment effect
- Hematological findings incidence and severity: No treatment effect
- Clinical biochemistry findings incidence and severity: No treatment effect
- Mortality: No treatment effect
- Gross pathology incidence and severity: No treatment effect
- Organ weight changes: No treatment effect
- Histopathology incidence and severity: No effect on ovaries, testes or accessory sex organs

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or

submitter: The submitter concludes that propylene carbonate had no effect on reproductive organs

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 2, key study

Remarks field for Data Reliability: Not a guideline study of reproductive effects, but indicates no effects would be expected.

REFERENCES (Free Text)

Margitich, D.J., 1989. Subchronic Oral toxicity in Rats. Pharmakon Research International, Inc. Final Report Ph 470-TX-001-88, pp. 1 – 158, plus two appendices.

OTHER

Last changed (administrative field for updating): 3/08/02 by ToxWorks

17) TOXICITY TO REPRODUCTION

TEST SUBSTANCE

Identity: Propylene Carbonate

METHOD

Method/guideline followed: Assessment of reproductive organs in a 14 week study

Type (one generation, two generation, etc.): Assessment of reproductive organs in a 14 week study

GLP (Y/N): Yes

Year (study performed): 1991

Species: Rat

Strain: Harlan F344

Route of administration - oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapor, gas, particulate), other: Aerosol inhalation

Doses/concentration levels: 0, 100, 500, 1000 mg/m³, diameter MMAD) = 4.9 +/- 2.5 gsd

Sex: Both

Control group and treatment: Clean air

Frequency of treatment: 93 Days

Statistical methods: One-way analysis of variance, followed by Dunnett's or Tukey's tests

Remarks field for Test Conditions:

- Test animals:

- Number, age, sex per dose for P, F1 and F2, if appropriate: 10 per sex per group, 47 days old

- Test design:

- Vehicle: None

- Parameters assessed during study P and F1 as appropriate:

- Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Daily
- Estrous cycle length and pattern (number of days spent in each phase): Not assessed
- Sperm examination (epididymal or vas sperm, concentration, motility, morphology): Not assessed

- Parameters assessed during study F1 and F2, as appropriate:

- Clinical observations performed and frequency (weight gain, growth rate, etc.): Weekly BW
- Organs examined at necropsy (macroscopic and microscopic): Ovaries, uterus, testes, accessory sex organs

RESULTS

NOAEL (NOEL) and LOAEL (LOEL) for P, F1 and F2, as appropriate: 100 mg/m³

Actual dose received by dose level by sex if known

Parental data and F1 as appropriate (toxic response/effects with NOAEL value):

Periocular swelling seen in a few males at 500 and 1000 mg/m³

Statistical results, as appropriate

Remarks field for Results:

- Body weight: No treatment effect
- Food/water consumption: No treatment effect
- Hematological findings incidence and severity: No treatment effect
- Clinical biochemistry findings incidence and severity: No treatment effect
- Mortality: No treatment effect
- Gross pathology incidence and severity: No treatment effect
- Organ weight changes: No treatment effect
- Histopathology incidence and severity: No effect on ovaries, testes or accessory sex organs

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or

submitter: The submitter concludes that propylene carbonate had no effect on reproductive organs

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 2, key study

Remarks field for Data Reliability: Not a guideline study of reproductive effects, but indicates no effects would be expected.

REFERENCES (Free Text)

Burleigh-Flayer, H.D., Nachreiner, D.J., Kintigh, W.J., 1991. Propylene carbonate: Fourteen-Week aerosol inhalation study on rats with neurotoxicity evaluation. Bushy Run Research Center Final Report 52-637, pp. 1 – 56, plus 12 appendices.

OTHER

Last changed (administrative field for updating): 3/08/02 by ToxWorks

18) DEVELOPMENTAL TOXICITY/TERATOGENICITY

TEST SUBSTANCE

Identity: Propylene carbonate

METHOD

Method/guideline followed

GLP (Y/N): Yes

Year (study performed): 1988

Species: Rat

Strain: Charles River Sprague-Dawley

Route of administration - oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapor, gas, particulate), other: Oral (gavage)

Doses/concentration levels: 0, 1000, 3000 and 5000 mg/kg/day

Sex: Females

Exposure period: Days 6-15 of gestation

Frequency of treatment: Once per day

Control group and treatment: Distilled water by gavage

Duration of test: Days 6-20 of gestation

Statistical methods: Anova, followed by Dunnett's

Remarks field for Test Conditions:

- Age at study initiation: 80-120 days
- Number of animals per dose per sex: 27
- Vehicle: None
- Clinical observations performed and frequency : Daily
- Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy): One male with one or two females until signs of copulation
- Parameters assessed during study (maternal and fetal): Daily toxicologic signs; body weight days 6, 9, 12, 15, 20; and food consumption days 0-6, 6-13, 13-20.
- Organs examined at necropsy (macroscopic and microscopic): Complete necropsy; number and location of viable fetuses, early and late resorptions, total implantations and corpora lutea, half of fetuses soft tissue analysis, other half skeletal analysis.

RESULTS

NOAEL (NOEL) and LOAEL (LOEL) maternal toxicity: 1000 mg/kg/day

NOAEL (NOEL) and LOAEL (LOEL) developmental toxicity: 5000 mg/kg/day

Actual dose received by dose level by sex if available

Maternal data with dose level (with NOAEL value). Provide at a minimum qualitative descriptions of responses where dose related effects were seen. Mortality, salivation, decreased activity, abnormal gait, dyspnea, cyanosis

Fetal data with dose level (with NOAEL value). Provide at a minimum qualitative descriptions of responses where dose related effects were seen. No effects

Statistical results, as appropriate

Remarks for Results:

- Mortality and day of death: at 3000 mg/kg/day: days 9 and 13; at 5000 mg/kg/day: days 10, 10, 11, 11, 14
- Number pregnant per dose level: At cesarean section, 27, 26, 23, 22 pregnant at 0, 1000, 3000 and 5000 mg/kg/day
- Number aborting: None

- Number of implantations: 15.4 15.2 15.6 14.9
- Pre and post implantation loss, if available: pre (%): 8.0 6.3 10.2 10.6
post (%): 4.7 9.7 5.2 11.7
- Number of corpora lutea (recommended): 17.0 16.3 17.5 16.6
- Duration of Pregnancy: Terminated day 20 of gestation
- Body weight: Decreased body weight gain at 5000 mg/kg/day: 53 g vs 77 g in control days 6-15
- Food/water consumption: Reduced food consumption at 3000 and 5000 mg/kg/day days 6-13
- Description, severity, time of onset and duration of clinical signs: Salivation, in some rats days 6-15, decreased activity in some rats days 6-15 at 3000 and 5000 mg/kg/day
- Hematological findings incidence and severity: Not examined
- Clinical biochemistry findings incidence and severity: Not examined
- Gross pathology incidence and severity: No adverse effects
- Organ weight changes, particularly effects on total uterine weight: Not examined
- Histopathology incidence and severity: Not examined
- Fetal data, provide at a minimum qualitative descriptions of responses where dose related effects were seen
- Litter size and weights:

size	14.6	13.6	14.7	13.2
weight	3.8	3.9	3.8	3.6
- Number viable (number alive and number dead)
- Sex ratio: % male 53 48 51 50
- Grossly visible abnormalities, external, soft tissue and skeletal abnormalities: No significant differences

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter. Submitter concludes that propylene carbonate does not induce developmental effects.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, key study

REFERENCES (Free Text)

Margitich, D.J. (1988). Developmental toxicity study in rats. Pharmakon Research International, Inc. Final Report PH 328-TX-001-88, pp. 1-44, plus 2 appendices.

OTHER

Last changed (administrative field for updating): 3/11/02 by ToxWorks